VOLUME 2

STUDY TITLE

Science Assessment Document for Tolerance Reassessment:
Alkyl Ammonium Chloride Salts

DATA REQUIREMENTS

NA

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STUDY COMPLETION DATE

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STATEMENT OF DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality is made for any information contained in this study on the basis of its falling within the scope of FIFRA §10(d)(1)(A), (B), or (C).

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GLP COMPLIANCE STATEMENT

This study was not conducted in accordance with the Good Laboratory Practice Standards as published in the U. S. Environmental Protection Agency Good Laboratory Practice Standards (FIFRA), 40 CFR 160 (*Federal Register*, Volume 54, No. 158, August 17, 1989) and differs in the following way(s):

This assessment, which is based upon literature in the public domain, is not a study and is not subject to the GLP Standards.

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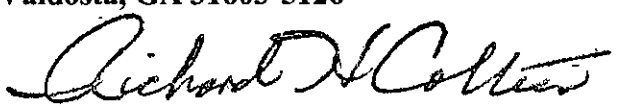
SIGNATURE: 

Richard H. Collier, Ph.D., Agent

DATE: **February 27, 2006**

Science Assessment Document for Tolerance Reassessment:

Alkyl Ammonium Chloride Salts

Submitted by the

Surfactants Task Force

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LANDIS INTERNATIONAL, INC.

February 27, 2006

Background:

The U.S. Environmental Protection Agency (EPA or the Agency) is in the process of reassessing tolerances for inert ingredients used in food-use pesticide products, a requirement of the Food Quality Protection Act (FQPA). The Surfactants Task Force (STF) has prepared this science assessment for tolerance reassessment of alkyl ammonium chloride salts (AACSs) to assist the Agency in this task.

This science assessment is based upon data in the public domain. It provides a robust assessment of the hazards associated with the use of AACSs as an inert ingredient in pesticide formulations. Both monoalkyl ammonium chloride salts (m-AACSs) and dialkyl ammonium chloride salts (d-AACSs) are discussed in this assessment.

After discussions with EPA staff, the STF identified the range of compounds designated as AACSs as a group or cluster for the purposes of tolerance reassessment on the basis of their chemical similarity. The structure of these compounds varies as to the length and number of alkyl chains attached to ammonium moiety and the nature of the counter ion. The variations in the side chains and counter ions account for the specific surfactant characteristics that lead to the choice of one member of this cluster over another for a particular surfactant application. As discussed in the following section of this report, the data we have reviewed indicate that these differences in the AACSs do not lead to differences in toxicological or environmental fate characteristics that are significant with respect to tolerance reassessment. Consequently, on the basis of their chemical, toxicological, and environmental similarity, it is appropriate to treat the AACSs as a group for the purposes of this assessment.

The counter ions of the AACSs are commonly used in other agricultural and consumer products. They have been previously considered by the Agency, found to present minimal risks and are not separately addressed in this report.

In this document the following abbreviations are used:

AACSs	alkylammonium chloride salts
m-AACSs	monoalkylammonium chloride salts
d-AACSs	dialkylammonium chloride salts
CSs	cationic surfactants
FND	fatty derived nitrogen
ATMACs	alkyltrimethylammonium chlorides
DADMACs	dialkyldimethylammonium chlorides
DADMAMSs	dialkyldimethylammonium methyl sulfates
DSDMACs	distearyldimethylammonium chlorides
DTDMACs	ditallowdimethylammonium chlorides
DDAC	didecyldimethylammonium chloride
DODAC	dioctyldimethylammonium chloride
CB	cetrimonium bromide
CC	cetrimonium chloride
SC	steartrimonium chloride

I. Executive Summary:

AACSs are considered in this science assessment. The database of toxicological data on AACSs in the open literature is somewhat limited. In spite of the limited quantity of public domain data, it is clear that AACSs in general exhibit limited toxicity to mammals by the oral and dermal routes of administration. Different members of the family of AACSs have been the subject of mammalian toxicity studies of various dosing durations. These studies include administration via the oral and dermal routes, as well as instillation into the eye.

This science assessment includes analysis of the properties of compounds closely related to AACSs where necessary for consideration of key aspects of the potential hazards of these compounds.

The grouping of compounds treated in this assessment is very similar to that considered as a category for assessment under the HPV challenge program in the American Chemistry Council HPV test plan, *Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge. [3]* We refer the Agency to that document for the SAR discussion and note that EPA agreed with the submitter's definition of the category.

II. Use Information:

This assessment is intended to support the reassessment of the four (4) tolerance exemptions for AACSs and their formaldehyde condensates listed in Table 1. Some of these are listed in multiple subsections at 40 CFR 180, each of which is noted in the table. The range of surfactant uses of the compounds which are the subject of this assessment are also shown in Table 1.

Each of the tolerance expressions includes a series of compounds for which there are multiple Chemical Abstracts Service (CAS) numbers. Examples of the specific compounds included in these tolerance expressions and which are evaluated in this science assessment are listed in Table 2, along with their CAS numbers and common descriptors. These lists may not be complete but represent the best efforts of the STF to determine those specific chemicals that are used in pesticide formulations. The Agency may find others in its files that are not available to the STF. Several AACSs are currently listed on the Agency's Inerts List 3.

Table 3 lists the AACSs considered in this assessment and some of their characteristics that are germane to the discussion of the reassessment of tolerance exemptions for this class of compounds. The first column is an item number provided for convenience of identifying a particular compound for the purposes of this table. In the second column, the tolerance expression (descriptor) in 40 CFR Part 180 is listed, if one exists for that item. The succeeding columns provide the Chemical Abstracts Service (CAS) Registry Number, the TSCA name, the 40 CFR Part 180 sub-part(s) under which the tolerance exemption was issued, the EPA Inerts List upon which the item is listed, an indication of whether the item is in the High Production Volume program, other names for the item, the chemical structure, and five columns for different types of study data. The last six columns contain the reference numbers from which data related to that item were cited.

As is the case with all surfactants, the surfactant properties of AACSs are derived from the hydrophilic and hydrophobic portions of these molecules. The tolerance exemptions that are the subject of this assessment (Table 3, items 1 through 4) share the same hydrophilic moiety, a quaternary ammonium salt. Chloride and methyl sulfate are the counter ions. The structures of these items are shown in column 9. The hydrophobic moiety of item 1 is a 3-lauramidopropyl group; other side chains of the ammonium moiety in item 1 are three methyl groups. The hydrophobic moiety of item 2 is a C8-18 hydrocarbon chain of natural origin (coconut, cottonseed, soya, or tallow); other side chains of the ammonium moiety in item two are methyl and two 2-hydroxyethyl groups. Item 3 is the ethoxylate of item 2 with 3-15 moles of poly(oxyethylene). The hydrophobic moiety of item 4 consists of one or two C8-18 hydrocarbon chain of natural origin (coconut, cottonseed, soya, tallow, or hogfat); the other side chains of the ammonium moiety in item 4 are two or three methyl groups.

We note the EPA agreed with the proposal of the American Chemistry Council in its HPV test plan, *Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge,* [3] to treat a very similar grouping as a single category based upon the SAR analysis in that document, to which we refer the Agency for its consideration of this assessment.

Table 1. Tolerance Exemptions Being Addressed in this Document

Tolerance Exemption Expression	40 CFR §180.	Use Pattern in Pesticides
(3-Lauramidopropyl) trimethylammonium methyl sulfate	920	Antistatic agent.
Methyl bis(2-hydroxyethyl)alkyl ammonium chloride, where the carbon chain (C_8-C_{18}) is derived from coconut, cottonseed, soya, or tallow acids.	920	Surfactants.
Methyl poly(oxyethylene) alkyl ammonium chloride, where the poly(oxyethylene) content is 3-15 moles and the alkyl group (C_8-C_{18}) is derived from coconut, cottonseed, soya or tallow acids.	920	Surfactants.
Mono- and dialkyl (C_8-C_{18}) methylated ammonium chloride compounds, where the alkyl group(s) (C_8-C_{18}) are derived from coconut, cottonseed, soya, tallow, or hogfat fatty acids.	920	Surfactants, related adjuvants of surfactants.

Table 2. Alkyl and Dialkyl Ammonium Chloride Salts

CAS Number	Common Descriptor	Inerts List
Monoalkyl		
112-00-5	Dodecyl trimethyl ammonium chloride	
112-02-7	Hexadecyl trimethyl ammonium chloride	3
112-03-8	Octadecyl trimethyl ammonium chloride	
3010-24-0	Octadecyl di(2-hyroxyethyl) methyl ammonium chloride	3
4574-04-3	Tetradecyl trimethyl ammonium chloride	
10108-87-9	Decyl trimethyl ammonium chloride	
10595-49-0	3-Lauramidopropanyl trimethyl ammonium chloride	
18448-65-2	Octadecyl di(2-hydroxyethyl) methyl ammonium chloride	
22340-01-8	Dodecyl di(2-hydroxyethyl) methyl ammonium chloride	
28724-32-5	Ethoxylated stearylmethyldipoly(oxyethylene) ammonium chloride	
28880-55-9	Ethoxylated oleylmethyldipoly(oxyethylene) ammonium chloride	
41572-20-7	Octyl di(2-hydroxyethyl) methyl ammonium chloride	
60687-90-3	Tetradecyl di(2-hydroxyethyl) methyl ammonium chloride	
61791-10-4	Ethoxylated cocoalkyl di(hydroxyethyl) methyl ammonium chloride	3
64755-05-1	Ethoxylated tallowalkyl di(hydroxyethyl) methyl ammonium chloride	3
67784-77-4	Tallowalkyl di(hydroxyethyl) methyl ammonium chloride	
68187-69-9	Ethoxylated hydrogenated tallowalkyl di(hydroxyethyl) methyl ammonium chloride	3
68607-27-2	Hydrogenated tallowalkyl di(hydroxethyl) methyl ammonium chloride	3
70750-47-9	Cocoalkyl di(hydroxyethyl) methyl ammonium chloride	3
Dialkyl		
107-64-2	Dioctadecyl dimethyl ammonium chloride	3
5538-94-3	Dioctyl dimethyl ammonium chloride	
7173-51-5	Didecyl dimethyl ammonium chloride	
10108-91-5	Ditetradecyl dimethyl ammonium chloride	

Table 1: Mapping Table for Alkyl Ammonium Chloride Salts and Related Compounds

Item No.	40 CFR Description	CAS Number	TSCA name	Tolerance Exemption	EPA Inerts List	HPV	Other name	Structure	Chem/Phys Properties Data	Acute Tox Data	Chronic/ Subchronic Tox Data	Metabolism Data	Other Tox Data	Environ Data
1	(3-Lauramidopropyl) trimethylammonium methyl sulfate	10595-49-0	1-Propanaminium, N,N,N-trimethyl-3-[(1-oxododecyl)amino]-, methyl sulfate	920	—	—	—	$(CH_3)_3N(CH_2)_3NHCO(CH_2)_{10}CH_3.CH_3SO_4$	—	—	—	—	—	—
2	Methyl bis(2-hydroxyethyl)alkyl ammonium chloride, where the carbon chain (C8-C18) is derived from coconut, cottonseed, soya or tallow acids.	3010-24-0	1-Octadecanaminium, N,N-bis (2-hydroxyethyl)-N-methyl-, chloride	920	3	—	Octadecyl di(2-hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=C18	—	—	—	—	—	—
		18448-65-2	9-Octadecen-1-aminium, N,N bis (2-hydroxyethyl)-N-methyl-, chloride	920	—	—	Oleyl di (2-hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=C18-cis-9-ene	—	—	—	—	—	—
		22340-01-8	1-Dodecanaminium, N, N-bis (2-hydroxyethyl)-N-methyl-, chloride	920	—	—	Dodecyl di (2-hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=C12	—	—	—	—	—	—
		41572-20-7	1-Octanaminium, N,N-bis (2-hydroxyethyl)-N-methyl-, chloride	920	—	—	Octyl di (2-hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=C8	—	—	—	—	—	—
		60687-90-3	1-Tetradecanaminium, N, N-bis (2-hydroxyethyl)-N-methyl-, chloride	920	—	—	Tetradecyl di (2-hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=C14	—	—	—	—	—	—
		67784-77-4	Quaternary ammonium compounds, bis(hydroxyethyl)methyltallow alkyl, chlorides	920	—	O-F	Tallowalkyl di (hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=tallow	—	—	—	—	—	—
		88607-27-2	Quaternary ammonium compounds, (hydrogenated tallow alkyl) bis (hydroxyethyl) methyl, chlorides	920	3	—	Hydrogenated tallowalkyl di (hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=tallow	—	—	—	—	—	—
		70750-47-9	Quaternary ammonium compounds, coco alkylbis (hydroxyethyl) methyl, chlorides	920	3	x	Cocoalkyl di (hydroxyethyl) methyl ammonium chloride	$CH_3N(CH_2CH_2OH)_2(R).Cl$, where R=coco	—	—	—	—	—	—

Table 1: Mapping Table for Alkyl Ammonium Chloride Salts and Related Compounds

Item No.	40 CFR Description	CAS Number	TSCA name	Tolerance Exemption	EPA Inerts List	HPV	Other name	Structure	Chem/Phys Properties Data	Acute Tox Data	Chronic/ Subchronic Tox Data	Metabolism Data	Other Tox Data	Environ Data
3	Methyl poly (oxyethylene) alkyl ammonium chloride, where the poly(oxyethylene) content is 3-15 moles and the alkyl group (C8-C18) is derived from coconut, cottonseed, soya or tallow acids.	28724-32-5	Poly (oxy- 1,2-ethanediyl), a,a'-[(methyloctadecylimino)di-2,1-ethanediyl]bis[w-hydroxy-, chloride	920	—	—	Stearylmethyldipoly(oxyethylene) ammonium chloride	$CH_3N((CH_2CH_2O)_nH)(R).Cl$, where R=C18	—	—	—	—	—	—
		28880-55-9	Poly (oxy- 1,2-ethanediyl), a,a'-[(methyl(9Z)9-octadecenylimino) di-2,1-ethanediyl]bis[w-hydroxy-, chloride	920	—	—	Oleylmethyldipoly(oxyethylene) ammonium chloride	$CH_3N((CH_2CH_2O)_nH)(R).Cl$, where R=C18	—	—	—	—	—	—
		61791-10-4	Quaternary ammonium compounds, coco alkylbis (hydroxyethyl) methyl, ethoxylated, chlorides	920	3	—	Ethoxylated cocoalkyl di (hydroxyethyl) methyl ammonium chloride	$CH_3N((CH_2CH_2O)_nH)(R).Cl$, where R=coco	—	—	—	—	—	—
		64755-05-1	Quaternary ammonium compounds, bis (hydroxyethyl)methyltallow alkyl, ethoxylated chlorides	920	3	—	Ethoxylated tallowalkyl di (hydroxyethyl) methyl ammonium chloride	$CH_3N((CH_2CH_2O)_nH)(R).Cl$, where R=tallow	—	—	—	—	—	—
		68187-69-9	Quaternary ammonium compounds, (hydrogenated tallow alkyl)bis (hydroxyethyl)methyl, ethoxylated chlorides	920	3	—	Ethoxylate hydrogenated tallowalkyl di (hydroxyethyl) methyl ammonium chloride	$CH_3N((CH_2CH_2O)_nH)(R).Cl$, where R=tallow	—	—	—	—	—	—
4	Mono- and dialkyl (C8-C18) methylated ammonium chloride compounds, where the alkyl group(s) (C8-C18) are derived from coconut, cottonseed, soya, tallow, or hogfat fatty acids.	112-00-5	1-Dodecanaminium, N,N,N-trimethyl-, chloride	920	—	O-F	Dodecyl trimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C12	3, 4	—	3	—	3	3
		112-02-7	1-Hexadecanaminium, N,N,N-trimethyl-, chloride	920	3	O-F	Hexadecyl trimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C16	3, 4	2, 3	2, 3	—	2, 3	3
		112-03-8	1-Octadecanaminium, N,N,N-trimethyl-, chloride	920	—	O-F	Octadecyl trimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C18	2, 3, 4	1, 2	1, 2, 3	—	3	3

Table 1: Mapping Table for Alkyl Ammonium Chloride Salts and Related Compounds

Item No.	40 CFR Description	CAS Number	TSCA name	Tolerance Exemption	EPA Inerts List	HPV	Other name	Structure	Chem/Phys Properties Data	Acute Tox Data	Chronic/ Subchronic Tox Data	Metabolism Data	Other Tox Data	Environ Data
		4574-04-3	1-Tetradecanaminium, N,N,N-trimethyl-, chloride	920	—	—	Tetradecyl trimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C14	—	—	—	—	—	—
		10108-87-9	1-Decanaminium, N,N,N-trimethyl-, chloride	920	—	—	Decyl trimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C10	—	—	—	—	—	—
		107-64-2	1-Octadecanaminium, N,N-dimethyl-N-octadecyl-, chloride	920	3	2-N	Dioctadecyl dimethyl ammonium chloride	$(CH_3)_2N(R)_2.Cl$, where R=C18	4	—	—	—	—	—
		1812-53-9	1-Hexadecanaminium, N-hexadecyl-N,N-dimethyl-, chloride	920	—	—	Hexadecyl dimethyl ammonium chloride	$(CH_3)_2N(R)_2.Cl$, where R=C16	—	—	—	—	—	—
		5538-94-3	1-Octanaminium, N,N-dimethyl-, N-octyl-, chloride	920	—	—	Dioctyl dimethyl ammonium chloride	$(CH_3)_2N(R)_2.Cl$, where R=C8	4	—	—	—	—	7
		7173-51-5	1-Decanaminium, N-decyl- N,N-dimethyl-, chloride	920	—	—	Didecyl dimethyl ammonium chloride	$(CH_3)_2N(R)_2.Cl$, where R=C10	3, 4	3	3	—	—	3, 7
		10108-91-5	1-Tetradecanaminium, N,N-dimethyl-N-tetradecyl-, chloride	920	—	—	Ditetradecyl dimethyl ammonium chloride	$(CH_3)_2N(R)_2.Cl$, where R=C14	—	—	—	—	—	—
		68002-59-5	Quaternary ammonium compounds, di-C14-18-alkyldimethyl, chlorides	920	—	O-F	C34H78NCl	$(CH_3)_2N(R)_2.Cl$, where R=C14-18	3	—	—	—	—	—
		68391-05-9	Quaternary ammonium compounds, di-C12-18-alkyldimethyl, chlorides	920	—	O-F	C32H79NCl	$(CH_3)_2N(R)_2.Cl$, where R=C12-18	3	—	3	—	—	—
		68783-78-8	Quaternary ammonium compounds, dimethylditallow alkyl, chlorides	920	3	O-F	—	$(CH_3)_2N(R)_2.Cl$, where R=tallow	—	—	3	—	3	3
		8030-78-2	Quaternary ammonium compounds, trimethyltallow alkyl, chlorides	920	3	O-F	Tallow trimethyl ammonium chloride	$(CH_3)_2N(R)_2.Cl$, where R=tallow	—	3	—	—	3	3

Table 1: Mapping Table for Alkyl Ammonium Chloride Salts and Related Compounds

Item No.	40 CFR Description	CAS Number	TSCA name	Tolerance Exemption	EPA Inerts List	HPV	Other name	Structure	Chem/Phys Properties Data	Acute Tox Data	Chronic/ Subchronic Tox Data	Metabolism Data	Other Tox Data	Environ Data
		61789-80-8	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, chlorides	920	—	O-F	—	$(CH_3)_2N(R)_2.Cl$, where R=tallow	---	—	3	—	—	3
		61789-77-3	Quaternary ammounium compounds, dicoco alkyldimethyl, chlorides	920	3	O-F	—	$(CH_3)_2N(R)_2.Cl$, where R=coco	---	—	—	—	3	—
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Ditallow, $C(16\text{-}18)_2$	$(CH_3)_2N(R)_2.Cl$, where R=tallow	---	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Dioctadecyl $C(18)_2$	$(CH_3)_2N(R)_2.Cl$, where R=C12	—	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Ditallow, $C(16\text{-}18)_2$ ^{14}[C]methyl	$(CH_3)_2N(R)_2.Cl$, where R=tallow	---	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Ditallow, $C(16\text{-}18)_2$ ^{14}[C]C1-alkyl	$(CH_3)_2N(R)_2.Cl$, where R=tallow	—	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Ditallow, $C(16\text{-}18)_2$ ^{14}[C]uniform-C	$(CH_3)_2N(R)_2.Cl$, where R=tallow	—	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Didecyl $C(10)_2$	$(CH_3)_2N(R)_2.Cl$, where R=C10	—	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Dioctadecyl $C(18)_2$	$(CH_3)_2N(R)_2.Cl$, where R=C18	—	—	—	—	—	1
		Not available	Not available	920	—	—	Dialkyldimethyl ammonium chloride, Ditallow $C(16\text{-}18)_2$ (hydrogenated)	$(CH_3)_2N(R)_2.Cl$, where R=tallow	—	—	—	—	—	1
		Not available	Not available	920	—	—	C8 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C8	—	—	—	—	—	1

Table 1: Mapping Table for Alkyl Ammonium Chloride Salts and Related Compounds

Item No.	40 CFR Description	CAS Number	TSCA name	Tolerance Exemption	EPA Inerts List	HPV	Other name	Structure	Chem/Phys Properties Data	Acute Tox Data	Chronic/ Subchronic Tox Data	Metabolism Data	Other Tox Data	Environ Data
		Not available	Not available	920	---	---	C10 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C12	---	---	---	---	---	1
		Not available	Not available	920	---	---	C12 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C12	---	1	---	---	---	1
		Not available	Not available	920	---	---	C14 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C14	---		---	---	---	1
		Not available	Not available	920	---	---	C16 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C16	---	1	---	---	5	1, 2
		Not available	Not available	920	---	---	C18 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C18	---	1	---	---	5	1
		Not available	Not available	920	---	---	C16-18 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C16-18	---	1	---	---	---	1
		Not available	Not available	920	---	---	14C labelled C18 alkyltrimethyl ammonium chloride	$(CH_3)_3N(R).Cl$, where R=C18	---	---	---	---	---	1
		Not available	Not available	920	---	---	Alkyltrimethyl ammonium chlorides	$(CH_3)_3N(R).Cl$	---	---	---	---	---	1
5	Not applicable	68002-58-4	Quaternary ammonium compounds, di-C14-18 alkyldimethyl, Me sulfates	none	---	O-F	C33H77NCl	$(CH_3)_2N(R)_2.CH_3SO_4$, where R=C14-18	3	---	---	---	---	---
6	Not applicable	61789-81-9	Quaternary ammonium compounds, bis(hydrogenated tallow alkyl) dimethyl, Me sulfates	none	3	O-F	---	$(CH_3)_2N(R)_2.CH_3SO_4$, where R=tallow	---	---	3	---	---	---
7	Not applicable	Not available	Not available	920	---	---	Dialkyldimethyl ammonium methyl sulfate, Ditallow $C(16-18)_2$	$(CH_3)_2N(R)_2.CH_3SO_4$, where R=tallow	---	---	---	---	---	1
8	Not applicable	57-09-0	1-Hexadecanaminium, N,N,N-trimethyl-, bromide	none	---	---	Cetrimonium Bromide	$(CH_3)_3N(R).Br$, where R=C16	---	---	---	2	---	---

A. Agricultural Uses of Alkyl Ammonium Chloride Salts

AACSs are antistatic agents, surfactants and related adjuvants of surfactants in pesticide formulations. [40 CFR 180.920] As cationic surfactants, AACSs are used as disinfectants and biocides, emulsifiers, wetting agents and processing additives. [1, 3] DDAC is FIFRA registered as an antimicrobial chemical with germicidal, fungicidal, and algaecidal activity. DDAC is used widely as a bactericide, fungicide, sanitizer, deodorant and disinfectant in the restaurant, dairy, food, laundry and medical industries. [3] As a disinfectant in biocidal products for food handling areas, DDAC is used at concentrations ranging from 3-25% active agent. [6]

The percentage of AACSs used as surfactants in pesticide formulations varies but the amount in the diluted formulations as applied in the field is typically well below 1%. The application and dilution rates are selected to assure that the treated surface is thoroughly covered.

B. FDA-Regulated and Industrial Uses of Alkyl Ammonium Chloride Salts

AACSs are cationic surfactants that are primarily used in fabric softeners, hair conditioners, and other hair preparations. [1] AACSs are also used in multifunctional liquid laundry detergents, antistatic sprays, germicides, deodorizers, industrial lubricants and corrosion inhibitors. [3] ATMAC is used in cosmetic products including hair conditioners, hair dyes, hair colors and other hair and personal care products. [1] CC is used in cosmetics as a cosmetic biocide, antistatic agent, surfactant cleansing agent, surfactant emulsifying agent, and a surfactant suspending agent while SC functions as an antistatic agent and surfactant. In cosmetics, CC is used at concentrations up to 10% in hair conditioners, tonics, dressing, grooming aids, and wave sets. In addition, CC is used in concentrations up to 5% in non-coloring hair rinses and moisturizing products and up to 1% in permanent waves and face and neck preparations. SC has been reported to be used at concentrations up to 1% in foundations. SC is also used in shampoos in conjunction with isopropyl alcohol to provide fluidity and clarity. [2]

III. Physical/Chemical Properties:

Physical/chemical property data on various AACSs have been reported by several sources. Table 4 contains physical/chemical properties for several representative mono- and di-alkyl ammonium chloride salts described in a HPV test plan. [3] Table 5 provides similar data provided by a chemical supplier. [4]

In addition, the Cosmetic Ingredient Review (CIR) reported in its review of AACSs used in certain cosmetic products that SC (CAS No. 112-03-8) is an amber liquid that contains approximately 50% active quaternary salts and has a molecular weight of 348.13. [2]

Table 4: Physical/Chemical Properties of Alkyl Ammonium Chloride Salts

CAS No.	Molecular Formula	Molecular Weight	Melting Point (°C)	Boiling Point (°C)	Vapor Pressure (mm Hg)	Partition Coefficient (log K_{ow})
Monoalkyl						
112-00-5	$C_{15}H_{34}NCl$	263	182	454	9.3 E-9	1.22
112-02-7	$C_{19}H_{42}NCl$	319	213	500	2.8 E-10	3.23
112-03-8	$C_{21}H_{46}NCl$	347	223	523	5.4 E-11	4.17
Dialkyl						
68002-58-4	$C_{33}H_{77}NCl$[a]	583	NA	NA	NA	NA
68002-59-5	$C_{34}H_{78}NCl$[b]	535	NA	NA	NA	NA
68391-05-9	$C_{32}H_{74}NCl$[a]	507	NA	NA	NA	NA
7173-51-5	$C_{22}H_{48}NCl$	361	229	535	2.3 E-11	4.66

a Based on average chain length = 15
b Base on average chain length = 16

Table 5: Physical/Chemical Properties of Alkyl Ammonium Chloride Salts

CAS No.	Physical State	Molecular Weight	Melting Point (°C)	Boiling Point (°C)	pH	Solubility in water
Monoalkyl						
112-00-5	White crystalline powder	263.89	>235	NA	NA	Soluble
112-02-7	Clear mobile solid	320.00	NA	100	6-9	Soluble
112-03-8	Clear mobile liquid	348.05	NA	100	6-9	Soluble
Dialkyl						
107-64-2	Light yellow paste (75%)	586.51	NA	100	6-9	Soluble
5538-94-3	White powder	305.97	NA	NA	NA	Freely soluble
7173-51-5	White powder	362.09	NA	NA	7	Freely soluble

IV. Hazard Assessment:

The public domain data used in this assessment were obtained primarily from databases of published literature accessed through the libraries of Florida State University, North Carolina State University, the University of Florida, and Valdosta State University. References were obtained through Internet searches utilizing the Google, Scirus, and Yahoo search engines. The list of all resources investigated is provided in Attachment A.

In the following sections of this document the public domain toxicity data on AACSs are summarized and the hazards associated with each potential route of exposure are assessed.

A. Toxicological Data:

Key comprehensive reviews of toxicological data on AACSs used in this assessment are the review by the CIR, *Final Report on the Safety Assessment of Cetrimonium Chloride, Cetrimonium Bromide and Steatrimonium Chloride [2]* and the American Chemistry Council

HPV test plan, *Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge [3]*. The latter reference provides robust summaries of the studies reviewed therein.

Acute Oral Toxicity

The acute oral toxicity of FND cationics indicates the chemicals may possess slight to moderate acute oral toxicity. The rat oral LD_{50s} range from approximately 200 to >2000 mg/kg. The acute oral LD_{50} for DDAC ranges from 60 to 400 mg/kg. [3] For CC, the reported rat oral LD_{50} is 250 to 300 mg/kg. In mice, the acute oral LD_{50} for SC over a 14-day observation period was 633 mg/kg for male mice and 536 mg/kg for female mice. [2]

Table 6 summarizes the acute oral toxicities of various ATMACs. [1]

Table 6: Acute Oral Toxicity of Alkyltrimethylammonium Chlorides

Surfactant	Species	LD_{50} (mg/kg body weight)
C_{16} ATMAC	Rat	400
C_{12} ATMAC	Rat	250-300
C_{18} ATMAC	Rat	1000
C_{18} ATMAC	Mouse	633
$C_{16\text{-}18}$ ATMAC	Rat	>500

Acute Dermal Toxicity

Two FND cationics (CAS No. 112-02-7 and 8030-78-2) failed to confirm an LD_{50} in rabbit acute dermal toxicity studies; however, a value slightly less than 4000 mg/kg was suggested. These results suggest the chemicals have minimal acute toxicity in rabbits via skin application. [3]

Skin Irritation

The skin irritation potential of CC has been tested both *in vitro* and *in vivo*. In an *in vitro* model for identifying skin-irritating chemicals, rat epidermal slices were exposed to CC (as supplied) and evaluated after 1, 4, and 24 hours. The irritation potential was determined by measuring the reduction in electrical resistance of the treated epidermal slices. CC was classified as a skin corrosive. In an *in vivo* study, the skin irritation potential of 0.1, 0.5, 1.2 and 2.5% CC was evaluated in six albino rabbits. The 0.1% concentration was non-irritating while the 2.5% concentration was severely irritating. The erythema and Eschar Index was 3.75 (maximum 4) and the edema Index was 2.0 (maximum 4). In another study, 0.2 mL volumes of either 1% or 10% CC were applied to the penile mucosa of one rabbit. After 24 hours, the overall irritant score was 0 for the 1% solution and 1.08 for the 10% solution. The possible maximum score for this test was 4. [2]

SC has been reported to the EPA as being severely irritating with a primary irritation index (PII) of 5.4. Clinical evidence of irritation included necrosis, sloughing of the skin, slight to

moderate erythema and very slight edema at 24 hours, and severe erythema and edema at 72 hours. The animal, dose and maximum possible irritation score were not specified. [2]

Ocular Irritation

The ocular irritation potential of AACSs has been evaluated in both guinea pigs and rabbits. The longer chained ATMACs are less irritating to rabbit eyes than the shorter alkyl chain homologues. [1] In one rabbit study, the ocular irritation potential of CC was evaluated using concentrations of 0.1, 0.5, 1.2, and 2.5%. CC (0.1 mL) was instilled into the conjunctival sac of one eye. The other eye served as a control. The eyes were examined 24 hours later both with and without fluorescein staining. All of the eyes were rinsed with 0.9% sodium chloride and examined 48 and 72 hours later. After 24 hours, the 0.1% concentration was non-irritating while the 2.5% concentration was moderately to severely irritating. After 72 hours, the 2.5% concentration was only mildly irritating. The 0.5% concentration was mildly irritating and cleared by 72 hours. After 6, 14, and 21 days, all of the eyes were restored to normal conditions. In another rabbit study, 1% and 10% solutions of CC were evaluated for ocular irritation potential. CC (0.2 mL) was instilled into one conjunctival sac of each of two rabbits. The eyes were examined 1, 24 and 48 hours later. The overall scores for the 1% and 10% solutions of CC were 3.6 and 47.5, respectively. The possible maximum score was 110. [2]

The ocular irritation potential of SC has also been evaluated in rabbit eyes. When 100 µL of 10% aqueous SC was instilled into the conjunctival sac of one eye of each of three rabbits, SC was slightly irritating. The total irritation score was 60.3 out of a possible maximum score of 110. In another study, SC was severely irritating to the eyes of nine rabbits. In this study, both rinsed and un-rinsed eyes had irritation for up to 13 days after the SC was administered. [2] In a third study, 100 µL of a 10% solution of SC was instilled into one eye of guinea pigs. The eyes were evaluated for ocular irritation after 0.5, 1, 2, 3, 4, 5, 6, and 24 hours. The SC was extremely irritating with a PPII of 96 (maximum 110). [1, 2]

Dermal Sensitization

The dermal sensitization of SC was evaluated using the Buehler assay in twenty (20) guinea pigs. In this experiment, the induction dose was 0.75% SC in 80% ethanol and the challenge dose was 0.5% SC in 80% ethanol. Fifteen of the animals had positive reactions. The average irritation score was 1.5; however, the maximum possible score was not reported. [2]

Summary of Acute Toxicity Endpoints

AACSs have been shown to present low acute toxicity by the oral and dermal routes of acute exposure. AACSs are not considered toxic or harmful in acute toxicity tests but are classified as irritating to the skin and eyes at high concentrations. [1, 2] It should be noted that the corrosivity findings with certain sulfonic acids are likely due to their low pH. The AACSs used in pesticides are in their ionized form at pHs near neutral.

Subchronic Effects

Several repeated dose toxicity studies conducted to assess the toxicity of AACSs were reviewed for the HPV test plan. [3] Each is discussed below.

In a 90-day oral toxicity feeding study in dogs, the NOAEL reported for a d-AACS (CAS No. 61789-80-8) was >100 mg/kg/day (highest dose tested). In this study, there were no effects related to the toxicity of the test substance.

A 13-week dermal toxicity study in rabbits using the same d-AACS (CAS No. 61789-80-8) was also conducted with dose levels of 10 and 140 mg/kg/day. No toxic effects other than skin irritation were observed at either dose level.

Rabbits were used in repeated dermal dose toxicity studies for an ATMAC (CAS No. 112-02-7) and a DADMAC (CAS No. 68391-05-9). Both studies were conducted using a single dose level of 10 mg/kg/day (limited by dermal irritation). The ATMAC study period was 28 days while the DADMAC study period was 13 weeks. No effects except mild irritation were noted in either study (NOAEL >10 mg/kg/day).

When a DADMAMS (CAS No. 61789-81-9) was evaluated in a rat subchronic study of 13 or 22 weeks duration, no NOEL was established; however the LOEL was reported to be 170 mg/kg/day.

DDAC (CAS No. 7173-51-5) has been evaluated in several repeated dose toxicity studies. At high doses such as 500 mg/kg/day, DDAC has been reported to be lethal to rats due to localized effects in the gastrointestinal tract. The NOAELs from two 90-day feeding studies in rats were 61 and 107 mg/kg/day. The NOAEL from a 13-week dermal toxicity study on this compound was >12 mg/kg/day.

In its review, the CIR described a 28-day subchronic dermal toxicity test in which rabbits were exposed to 2 mL/kg/day of CC. The CC was applied to the clipped and abraded skin of the rabbits for 6.5 to 7.0 hours, 5 days a week for a total of 4 weeks. No deaths occurred and there was no evidence of toxicity or hematological changes. [2]

Collectively, the studies discussed above provide evidence for low to limited subchronic toxicity for the AACSs tested.

Chronic Toxicity

The HPV test plan reviewed three chronic toxicity studies on DDAC (CAS No. 7173-51-5). The NOAEL in a 52-week study on dogs was 10 mg/kg/day. The NOAEL in a rat chronic study was 32 mg/kg/day. The NOAEL in a chronic study in mice was 76 mg/kg/day. [3]

In its review, the CIR described a 1-year chronic toxicity study in which CB was administered to rats in drinking water at doses of 10, 20, and 45 mg/kg/day. The only effect noted was body weight gain at the 45 mg/kg/day dose. [2]

The studies discussed above provide evidence for limited chronic toxicity for the AACSs tested.

Reproductive and Developmental Toxicity

The HPV test plan described potential reproductive effects of AACSs as assessed by the evaluation of reproductive organs in repeat dose toxicity studies in dogs and rats. No effects on the gonads or other reproductive organs were observed for CAS No. 61789-80-8 in dogs and CAS No. 61789-81-9 in rats. The NOELs for reproductive screening were >100 mg/kg/day and >750 mg/kg/day, respectively. In a two-generation reproductive study in rats, the NOEL for DDAC was approximately 56 mg/kg/day for adult and offspring toxicity. No reproductive effects were found. [3]

The HPV test plan also described potential developmental toxicity studies conducted for various AACSs, including the following CAS Nos.: 112-00-5, 112-02-7, 112-03-8, 68783-78-8 and 61789-81-9. Each of these studies is briefly described below. [3]

> When CAS No. 112-00-5 was tested, the oral NOEL for maternal and developmental toxicity was 24 mg/kg/day. No embryo toxicity, fetal toxicity or teratogenicity was observed.
>
> The percutaneous NOEL for maternal and developmental toxicity in rabbits was >10 mg/kg/day for CAS No. 112-02-7 and >12.5 mg/kg/day for CAS No. 112-03-8 in rats. No embryo or fetal toxicity was observed in either study. Note that the dose was limited by irritation.
>
> The NOEL for maternal toxicity for CAS No. 68783-78-8 in rats was >500 mg/kg/day via gavage. No maternal toxicity NOEL was established when the experiment was conducted via diet. The developmental NOEL for both studies (gavage and diet) was >500 mg/kg/day.
>
> When CAS No. 61789-81-9 was tested in a similar manner, the maternal and developmental NOELs were 500 or 475 mg/kg/day via gavage or diet, respectively.
>
> When DDAC was the test chemical, the NOELs for rabbits in two studies were 1.0 and 3.0 mg/kg/day for maternal and developmental toxicity, respectively.
>
> When the same test was conducted in rats, the results were 1.0 and 20.0 mg/kg/day, respectively. No teratogenic effects were observed for either species.

The HPV test plan authors concluded that the compounds in this class are unlikely to cause reproductive effects and are not developmental toxicants.

In its review, the CIR described reproductive and developmental toxicity studies for CC. In one study, twenty (20) pregnant rabbits were given topical applications of CC at concentrations of 0.5, 1.0, and 2.0% for 2 hours on days 7 to 18 of gestation. No statistically

significant changes were observed for maternal body weight, mean body weight gain, or feed consumption. There were no significantly different reproductive parameters, incidence of fetal malformations or developmental variations. The authors concluded that CC is not maternally toxic, embryotoxic, or teratogenic. [2]

Review articles also reported on a study in which the embryotoxic and teratogenic potential of SC was evaluated in rats. Concentrations of 0.9, 1.5, 2.5% SC were applied to the shaved skin of pregnant rats on days 6 to 15 of gestation. No embryotoxic effects were seen and there was no increase in fetal malformations. [1, 2]

Collectively, the studies discussed above provide adequate evidence that the AACSs are neither developmental nor developmental toxicants.

Mutagenicity

In short term genotoxicity assay system tests of over 200 surfactants (including C_{16} and C_{18} ATMAC), all of the surfactants were shown to have negligible potential to cause genetic activity. The assays performed were *Salmonella*/microsome mutation assays, bacterial DNA repair tests, mitotic recombination in *Saccharomyces cervisiea*, mouse lymphoma cell-mutation assays, unscheduled DNA synthesis and sister chromatid exchange assays in mammalian cells, mammalian chromosome damage tests *in vitro* and *in vivo*, dominant lethal tests in rodents and mammalian cell-transformation tests.[5]

The HPV test plan described the following mutagenicity studies (*Salmonella* reverse mutation assays) conducted for various FND Cationic Category chemicals. One m-AACS, CAS No. 112-00-5, was negative for mutations in a standard assay. Three tests for two other m-AACSs, CAS No. 112-02-7 and 112-03-8, were also negative for mutagenic activity. A test for a d-AACS, CAS No. 61789-77-3, was also negative for four tester strains evaluated. Inconsistent results were observed for the m-AACS CAS No. 8030-78-2. For this chemical, one test indicated no mutagenic activity and one test showed a three-fold increase in back mutations in one cell line tested. A nonstandard *in vitro* test that examined morphological changes and an *in vivo* mouse micronucleus assay were negative for CAS No. 112-02-7 and CAS No. 68783-78-8, respectively. No mutagenic effects, no effect on DNA synthesis, and no chromosomal aberrations were observed for DDAC. The authors concluded that the AACSs are unlikely to have mutagenic activity. [3]

The CIR review described the following mutagenicity studies. CC (0.05 to 1 μg/plate) was negative in an Ames test using *Salmonella typhimurium* strains TA98 and TA100 with and without metabolic activation. When CC at concentrations of 5 to 10 μg/plate was tested, negative results were obtained in the presence of S9 activation; however, the concentrations were toxic to the bacteria without metabolic activation. In a third Ames test, CC was tested with *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538. The concentrations in this study were 1, 5, 25, 125, and 625μg/plate. CC was negative both with and without activation for all of the strains tested. When 50% CC was tested using *Salmonella typhimurium* strains TA1535, TA1537, and TA1538 at concentrations of 0.005 to 5.0μg/plate, CC was not mutagenic in any of the strains tested either with or without activation. CC was also tested in forward-mutation and reverse-mutation tests using E. coli

strain 343/113. The concentrations of CC in this study were 1, 10, and 50µg/mL. CC did not increase the number of mutant colonies from cell cultures incubated in different mediums for 20, 40, or 72 hours. In another study, CC (24-26% active ingredient) was tested in a chromosome aberration assay using Chinese hamster V79 cells. Various concentrations and incubation times were tested. CC was not mutagenic in all of the tests, both with and without metabolic activation. An *in vitro* cell transformation assay was used to test the carcinogenic potential of CC. At doses of 0.05, 0.1, 0.5, and 1.0 µg/mL, CC did not cause transformation. The authors concluded that the mutagenicity data were uniformly negative and that, given certain use limits for products applied and left on the skin but without limits on rinse-off products, the data were more than adequate to preclude any potential carcinogenic effects. [2]

Collectively, the studies discussed above provide adequate evidence that the AACSs are not mutagenic.

Absorption, Distribution, and Metabolism

The HPV test plan reported distribution data from a study performed using the d-AACS (CAS No. 61789-80-8). In this study, rats were fed 2800 ppm of this chemical for 90 days and 16% of the consumed dose was found in the excreta of males while 6% was found in the excreta of females. [3]

The CIR review described various absorption, distribution, and metabolism studies regarding Cetrimonium Bromide (CB). Each of theses studies is described below. [2]

> Female rats were given 0.8 mg/kg ^{14}C-CB by gastric intubation and sacrificed after 2, 4, 8, 24, 72 or 96 hours. Another set of similarly treated animals were kept in metabolism cages and urine and feces were collected at 4 hour intervals for 3 days. Expired CO_2 was collected at 4 hour intervals for 24 hours and bile samples were collected at 2 hour intervals for 12 hours. The researchers concluded CB was poorly absorbed by the intestines since 80% of the administered radioactivity was found in the gastrointestinal tract after 8 hours, 2% was excreted in the bile during the first 12 hours, and very small amounts were found in the blood plasma at day 4. In addition, 92% was excreted in the feces and 1% was eliminated in the urine by day 3. There was no radioactivity detected in the expired CO_2 and thin-layer chromatography showed the CB was metabolized to some extent.
>
> The rate and route of excretion of CB was determined after the intravenous administration of CB in 2 male rats. The rats were injected with 0.023% ^{14}C-CB in 0.9% aqueous NaCl and placed in a metabolism cage for 24 hours. After 24 hours, 58.9% of the radioactivity was found in the urine, 11.6% in the feces and 15.3% in the tissues for a total of 85.8%. The researchers reported that unidentified metabolites were found in the urine, unchanged CB was found in the feces and no radioactivity was found in the expired air.
>
> When 3 male rats were given 0.135 to 0.174% ^{14}C-CB via a jugular cannula, the radioactivity was 24.89% in the liver and 5.54% in the kidneys of two rats that were

sacrificed after 15 minutes of administration. In the third rat, the radioactivity in the blood decreased after 30 minutes and after 5 hours, very little radioactivity could be detected (2.08% in the liver and 0.36% in the kidneys).

When 3 rats were given 0.29% ^{14}C-CB in 0.9% aqueous NaCl subcutaneously, most of the radioactivity was eliminated in the urine in the first 24 hours. After 48 hours, a total of 96.2% was recovered: 68.1% in the urine, 14.1% in the feces and 13.9% in the tissues.

An unspecified number of rats were given a single aqueous dose of 2.9×10^{-4} mol/kg CB, 1.5×10^{-3} mol/kg sodium nitrate, or a combination of the two by gavage. After 2 hours, no significant changes were observed for serum alkaline phosphatase, glutamic-pyruvic transaminase, and total bilirubin concentration.

The absorption of CB was tested in 5 male rats. A concentration of 0.5, 1 or 3% ^{14}C-CB was applied to the clipped skin of the rats using non-occlusive methods. The group with 1% CB was observed for 72 hours while the other two groups were observed for only 48 hours. The percutaneous absorption for the 0.5, 1, and 3% groups were 0.093%, 0.59%, and 3.15%, respectively. The calculated total daily absorption for the three groups was 0.0004, 0.002, and 0.012 mg/kg/day, respectively.

The available studies indicate that AACSs are likely to be poorly absorbed from the intestinal tract. The studies using intravenous and subcutaneous dosing indicate that absorbed AACSs may be expected to be rapidly excreted in urine.

Ancillary effects

Even though AACSs can be significantly irritating to both the skin and eye, the adverse effects of some CSs on proteins may be reversible. CSs can interact with proteins or peptides by polar and hydrophobic binding. The polar interactions can result in electrostatic bonds between the positively charged surfactant molecule and the negatively charged groups of the protein molecule. [3]

Summary of Toxicological Effects

AACSs exhibit low acute toxicity via the oral and dermal routes and limited toxicity in all exposure durations tested except at doses far beyond those that could reasonably be expected from their use in pesticides. The data on AACSs is similar to that obtained on other classes of surfactants previously assessed either by EPA or by the STF, all of which exhibit low acute toxicity, show no likelihood of significant toxicity in subchronic and chronic studies, and are not teratogenic or mutagenic. [1-3, 5]

B. Special Considerations for Infants and Children:

There are no data that point to any concern for increased risk to infants or children from exposure to AACSs. Further, none of the closely related compounds show such effects. [1-3, 5] AACSs are widely used in consumer products used by children and adults, including

such products as various liquid laundry detergents, fabric softeners, disinfectants and personal care products. [1-3] These products have a long, safe use history. Consequently, no safety factor has been used in this document for special considerations for toxicity to infants and children and such a safety factor is not necessary.

V. Exposure Assessment:

Exposure to the AACSs may occur through FDA-approved uses. AACSs are used in fabric softeners, hair conditioners, other hair preparations, multifunctional liquid laundry detergents, antistatic sprays, germicides, deodorizers, industrial lubricants and corrosion inhibitors. [1,3] ATMAC is used in cosmetic products including hair conditioners, hair dyes, hair colors and other hair and personal care products. [1] CC is used in cosmetics as a cosmetic biocide, antistatic agent, surfactant cleansing agent, surfactant emulsifying agent, and a surfactant suspending agent while SC functions as an antistatic agent and surfactant. [2]

Human exposure to AACSs from FDA-approved sources, both from foods and from cosmetics, may be reasonably expected to be much greater than that for the use of these compounds in pesticide formulations. Except in cases of extreme dosages, AACSs are of low toxicity to mammals. Consequently, there is no reason to expect that the use of these compounds in pesticide formulations will present any significant hazard, and no quantitative exposure assessment has been performed.

VI. Risk Characterization:

Based upon the hazard aspect only, AACSs present little risk in any exposure scenario because of their inherent low toxicity. The exposures expected from the use of these compounds in pesticide formulations are expected to also be low, much lower than those already approved by the FDA for the cosmetic uses of AACSs.

The minimal hazard profile of the AACSs is similar to the hazard profiles of other groups of surfactants for which the US EPA has already reviewed the corresponding data and approved the reassessment of tolerances. [40 CFR 180] These documents indicate that the US EPA has already reviewed and approved tolerances for fatty acids, fatty alcohols, glycerol fatty acid esters, and certain PEG sorbitan fatty acid esters, that have structural and functional similarity to the AACSs. Although these groups are different enough that it is appropriate to separately consider the AACSs, the data that supported the approval of these similar compounds is consistent with the low toxicity of AACSs. Consequently, although the universe of data on the AACSs is not large, when considered along that of other similar compounds, it is sufficient to conclude that the AACSs present minimal hazards from their uses in pesticide formulations.

When all the available hazard data are considered, and the exposure to AACSs from their uses in pesticide formulations are compared to the FDA-approved cosmetic uses, as EPA concluded in the case of their review of the glycerol fatty acid esters, we conclude that it is

unlikely that the uses of AACSs in pesticide formulations will pose a significant hazard to the general public or any sub-population group. Any exposure from the use of the AACSs as inert ingredients in pesticide formulations may reasonably be expected to be well below any level that could cause an adverse effect. Consequently, this qualitative assessment has been performed in lieu of a quantitative risk assessment.

VII. Environmental Fate/Ecotoxicity/Drinking Water Considerations:

A. *Environmental Fate Characterization:*

The biodegradation of ATMACs may be initiated by fission of the C-N bond in which the alkyl chain or methyl group is cleaved from a tertiary amine or by ω-oxidation in which the far end of the alkyl chain is first oxidized to a carboxylic acid. Biodegradation could then proceed via β-oxidation. Studies involving a *Xanthomonas* sp. that is capable of biodegrading $_{10}$ATMAC support both degradation models. In one study, 9-carboxynonyl- and 7-carboxyheptyltrimethyl- ammonium chloride were detected during the growth of a *Xanthomonas* sp. on $_{10}$ATMAC.

The ultimate biodegradability of ATMAC has been examined in various standard biodegradation tests. The recalcitrance of ATMAC in screening tests has been shown to increase with increasing chain length. The biodegradability of various chain lengths of ATMAC during a 10 day experiments were as follows: 73% of ThOD for C_8, 63% for C_{10}, 59% for C_{12}, 35% for C_{14}, and 0% for C_{16} and C_{18}. In aerobic screening tests, ATMAC was ultimately degraded; however, it is difficult to verify whether or not the OECD criteria for ready biodegradability were fulfilled since information on the inoculum used in the test was not supplied. When C_{16} ATMAC (10 mg/L) was used in a ready biodegradability test, 40% of the ThOD was reached during 28 days without acclimation of the inoculum. The bacterial toxicity and absorptive properties of AACSs may result in an underestimation of the biodegradation potential in the aquatic environment. The presence of equimolar amounts of anionic surfactants may prevent the bacterial toxicity of longer chained ATMACs. ATMAC has been shown to be extensively mineralized when complexed with the anionic surfactant, linear alkylbenzene sulfonate (LAS). In one study, a mixture of C_{18} ATMAC and LAS resulted in a mineralization corresponding to 81% of ThOD in 25 days. C_{18} ATMAC at 20 mg/L was shown to inhibit the endogenous CO_2 production thereby preventing biodegradation. When ^{14}C-labelled C_{18} ATMAC was added to the SCAS system, rapid and extensive mineralization was observed. In another study, ^{14}C-labelled C_{18} ATMAC showed an extensive mineralization in river water. In this study, $^{14}CO_2$ was found that corresponded to more than 60% and 75% of the added ^{14}C after 7 and 21 days, respectively. The half-life of C_{18} ATMAC was calculated to be 2.2 days in acclimated river water, thus supporting the rapid transformation of ATMAC. Researchers suggest that no metabolites with appreciable half-lives are formed from the degradation of C_{18} ATMAC. [1]

The ultimate biodegradability of DADMAC has also been evaluated in several studies. Similar to ATMAC, the recalcitrance of DADMAC also increases with alkyl chain length. In a 10-day MITI test of various DADMACs resulted in 50% of ThOD for $C_{(10)2}$ and 0% for alkyl chain lengths from $C_{(12)2}$ to $C_{(18)2}$. DADMACs with branched alkyl chains are expected

to degrade more slowly than those with linear alkyl chains. Complete removal of $C_{(10)2}$ DADMAC was observed within 4 days when columns were inoculated with pure bacterium that was able to utilize $C_{(10)2}$ DADMAC for growth. When a similar experiment was conducted for $C_{(18)2}$ DADMAC, the transformation period was 8 days rather than 4. In another study, $C_{(16\text{-}18)2}$ was transformed with in columns with river water in 14 days; therefore the researchers concluded that microorganisms capable of primary degradation of DADMAC are common. From this data, the researchers suggest that the poor degradability that is evident in screening tests is not necessarily due to the recalcitrance of DADMAC. Other factors such as toxicity and a slow desorption of the cationic surfactants from the surfaces may limit biodegradation. When ^{14}C-labelled $C_{(16\text{-}18)2}$ DADMAC complexed with LAS was added to semi-batch reactors, the entire DADMAC molecule was ultimately biodegraded. A short-chained $C_{(8)2}$ DADMAC has also been reported to be ultimately biodegraded in acclimated river water. The half-lives calculated were 4.9 days in the presence of sediment and 13.8 days without sediment. Table 7 summarizes the results of various studies conducted for the ultimate and primary biodegradation of DADMACs under aerobic conditions. [1]

Table 7: Ultimate and primary biodegradability of Dialkyldimethyl Ammonium Chlorides (DADMACs) under Aerobic Conditions

DADMAC	Test	Duration	Result
Ditallow $C_{(16\text{-}18)2}$	Closed bottle test	283 days	68% ThOD
Dioctadecyl $C_{(18)2}$	Sturm test	33 days	4% $ThCO_2$
Ditallow, $C_{(16\text{-}18)2}$ [^{14}C]methyl	Semi-batch reactor	39 days	40; 53% $^{14}CO_2$ 72; 77% removal (primary)
Ditallow, $C_{(16\text{-}18)2}$ [^{14}C]C_1-alkyl	Semi-batch reactor	39 days	31% $^{14}CO_2$ 61% removal (primary)
Ditallow, $C_{(16\text{-}18)2}$ [^{14}C]uniform-C	Semi-batch reactor	39 days	22; 31% $^{14}CO_2$ 59%; 81% removal (primary)
Didecyl $C_{(10)2}$	Silica gel column, pure culture	4 days	100% removal (primary)
Dioctadecyl $C_{(18)2}$	Silica gel column, pure culture	8 days	100% removal (primary)
Ditallow $C_{(16\text{-}18)2}$ (hydrogenated)	Silica gel column, river water	14 days	Removal of parent substrate; extent not stated in reference

In the reactors, the methyl groups bound to the quaternary nitrogen were more susceptible to biodegradation than the carbons in the alkyl chains. DADMAC have been shown to degrade at a slower rate than ATMAC. [1]

There is limited data on the anaerobic degradability of AACSs. In an anaerobic digester, the concentration of quaternary ammonium salts does not decrease. In one anaerobic biodegradability test, 14.0 mg C/l of C_{16} ATMAC was toxic to the anaerobic bacteria. [1] CC has been reported to have inhibitory effects on activated sludge microorganisms *Photobacterium phosphoreum* and *Spirillum volutans*. [2]

Bioaccumulation studies of ATMAC have been performed with fathead minnow by using ^{14}C-labelled model compounds. The bioconcentration of ATMAC are hydrophobicity dependent. In one study, the concentration ratio for C_8 was 2.4, for C_{12} was 35 and for $C_{16\text{-}18}$ was 1,962. The high concentration ration for $C_{16\text{-}18}$ may represent both the intact surfactant

and its metabolites. The bioconcentration of DADMAC has been studied in both bluegill sunfish and fathead minnow. The CR for $C_{(16\text{-}18)2}$ DADMAC was determined to be 32 for bluegill sunfish. The CR for $C_{(18)2}$ for fathead minnow was 104. [1]

B. Ecotoxicity and Ecological Risk Characterization:

Numerous ecotoxicity studies have been performed on AACSs with different aquatic organisms including fish, crustaceans, invertebrates and algae. Chronic toxicity to aquatic organisms varies considerably for AACSs. One report indicated the chronic toxicity to aquatic organisms ranged from 4.15 µg/L to 12.7 mg/L. The composition of the test water can dramatically affect the toxicity of the test substance. This may be due to the fact that cationic substances in the environment instantaneously form complexes with naturally occurring negatively charged constituents in sewage, soils, sediments and with dissolved humic substances in surface waters which results in a reduced bioavailability. [3]

Various model prediction studies for fish toxicity have been conducted that can be compared to measured values. When CAS No. 112-00-5 was studied, model prediction results were similar to measured results, 9.77 mg/l for the model and 6.0 mg/l measured. For DDAC, the model predicted 2.3 mg/L and the measured values ranged from 0.3 to 2.8 mg/L. The models under predicted the toxicity for CAS No. 112-02-7. The model predicted 2.24 mg/l for this chemical and the measured value was 0.07 mg/L. Predicted values for aquatic invertebrates were similar to those for fish; however, they were not comparable to the measured values. For example, CAS No. 112-03-8 was predicted to have no toxicity at solubility and the measured value was 0.07 mg/L. Table 8 provides a comprehensive summary of the ecotoxicity data reviewed in the FND Cationics Category HPV Chemicals Challenge Test Plan. [3]

ATMACs have been shown to be acutely toxic to aquatic invertebrates. The EC_{50}/LC_{50} values for alkyl chain lengths of C_{16} have been reported below 1 mg/L. When the freshwater clam *Corbicula fluminea* was exposed to C12 ATMAC, minor and transient effects on length gain were observed at 43 µg/L during weeks 2-4 and 6-7 but the effects were not evident at 8 weeks (end of the study). Algae also appear to be very sensitive to cationic surfactants. The EC50 of ATMAC to algae has been reported to be below1 mg/L. The effects of various ATMAC on algae, invertebrates and fish are summarized in Table 9. [1]

Similar to ATMACs, DADMACs are toxic to algae, aquatic invertebrates and fish. The lowest EC_{50}/LC_{50} values are also below 1 mg/L. The effects of DADMACs on algae, invertebrates and fish are summarized in Table 10. [1]

The OPP Pesticide Ecotoxicity Database lists various ecotoxicity studies for both DODAC (CAS No. 5538-94-3) and DDAC (CAS No. 7173-51-5), which are summarized in Table 11. [7]

Table 8: Ecotoxicity Data for Various AACSs

CAS No.	Acute Toxicity to Fish LC_{50} (mg/L)	Acute Toxicity to Invertebrates EC_{50} (mg/L)[a]	Toxicity to Aquatic Plants EC_{50} (mg/L)	Chronic Toxicity to Aquatic Species (mg/L)[b]
Monoalkyl				
112-00-5	6.0	0.39 0.345	NA	NOEC fish= 0.5 to >1.25 LC_{50} CD= 0.31 LC_{50} CD= 0.30-0.45 NOEC CD= 0.05-0.25 NOEC CD (Survival)= 0.25 NOEC Clam ≈ 0.046 (8 week) EC_{50} Rotifer= 0.23 (48 hours)
112-02-7	0.07	NA	NA	EC_{50} Rotifer= 0.067 (48 hours)
8030-78-2	NA	0.0126-0.0989	NA	NOEC Daphnia= 0.0068-0.0991 (21days)
112-03-8	0.07	NA	NA	NA
Dialkyl				
7173-51-1	0.3-2.4 (48 hr) .027-2.8 (96 hr)	0.09 (daphnia) 0.07 (mysid)	≈3.5	NA
68783-78-8	0.62 to >24 24	CD= 0.54-1.23 DM= 0.19- 1.06 Oyster= 2.0 MS= 0.22 (96 hr) Shrimp= 36 Crab>50	1.12 0.21 to ≤10[c]	NOEC Fish= 12.7 LC_{50} CD= 0.70 LC_{50} CD= 0.82
61789-80-8	1.33 4.22 3.4 0.29-14	0.065-3.6	0.026-1.8	NA

[a]Values are for 48-hours unless specified
[b]Values are for 7-day studies unless otherwise noted
[c]Values are algaestatic concentrations for several species

CD= Ceriodaphnia
DM= Daphnia Magna
MS= Mysid shrimp

Table 9: Effects of Alkyltrimethylammonium Chlorides to Algae, Invertebrates and Fish

Surfactant	Organism	Species	Duration	EC_{50}/LC_{50} (mg/L)
C_{12} ATMAC	Algae	*Selenastrum capricomutum*	96 hr	0.19
C_{12} ATMAC	Algae	*Microcystis aeruginosa*	96 hr	0.12
C_{12} ATMAC	Algae	*Navicula pelliculosa*	96 hr	0.20
C_{16-18} ATMAC	Algae	*Dunaliella sp.*	24 hr	0.38 (0.33-0.45)[A]
C_{16-18} ATMAC	Algae	*Chlorella pyrenidosa*	96 hr	0.28 (0.22-0.26)[A]
ATMAC[B]	Crustacea	*Daphnia magna*	Not stated	1.2-5.8
C_{16} ATMAC	Crustacea	*Gammarus sp.*	48 hr	0.1 (0.08-0.14)[A]
C_{16} ATMAC	Flatworm	*Drugesia sp.*	48 hr	0.68 (0.58-0.80)[A]
C_{16} ATMAC	Oligochaete	*Dero sp.*	48 hr	0.22 (0.13-0.36)[A]
C_{12} ATMAC	Bivalve	*Corbicula fluminea*	56 days	LOEC: 0.18-0.24[C] NOEC: 0.043-0.049[C]
ATMAC[B]	Water snail	*Planorbis corneus*	Not stated	0.73-23
ATMAC[B]	Fishes	*Idus melatonus*	Not stated	0.36-8.6

[A]95% confidence limits
[B]The ranges include tests with C_{12}, C_{14}, C_{16}, C_{18} and C_{20-22}
[C]Effect concentration based on measured concentrations

Table 10: Effects of Dialkyldimethylammonium Chlorides to Algae, Invertebrates and Fish

Surfactant	Organism	Species	Duration	EC_{50}/LC_{50} (mg/L)
DADMAC Ditallow $C_{(16-18)2}$	Algae	*Dunaliella sp.*	24 hr	18 (13-24)[A]
DADMAC Ditallow $C_{(16-18)2}$	Algae	*Chlorella pyrenidosa*	96 hr	6.0 (5.5-6.5)[A]
DADMAC Ditallow $C_{(16-18)2}$	Algae	*Selenastrum capricomutum*	96 hr	0.06
DADMAC Ditallow $C_{(16-18)2}$	Algae	*Selenastrum capricomutum*	120 hr	0.23[B] (0.16-0.32)[A]
DADMAMS Ditallow $C_{(16-18)2}$	Algae	*Selenastrum capricomutum*	120 hr	0.1-0.5[B]
DADMAC Ditallow $C_{(16-18)2}$	Algae	*Microcystis aeruginosa*	96 hr	0.05
DADMAMS Ditallow $C_{(16-18)2}$	Algae	*Microcystis aeruginosa*	120 hr	0.1[B]
DADMAC Ditallow $C_{(16-18)2}$	Algae	*Navicula pelliculosa*	96 hr	0.07
DADMAC Ditallow $C_{(16-18)2}$	Crustacea	*Daphnia magna*	48 hr	0.19[C] (0.15-0.24)[A]
DADMAC Ditallow $C_{(16-18)2}$	Crustacea	*Daphnia magna*	48 hr	0.16-1.06
DADMAC Dioctadecyl $C_{(18)2}$	Crustacea	*Daphnia magna*	48 hr	0.16[C]
DADMAC Ditallow $C_{(16-18)2}$	Water flea	*Ceriodaphnia dubia*	48 hr	0.54[C] (0.22-0.80)[A]
DADMAC Ditallow $C_{(16-18)2}$	Crustacea	*Mysidopsis bahia*	96 hr	0.22[C] (0.17-0.30)[A]
DADMAC Ditallow $C_{(16-18)2}$	Invertebrate	*Chironomus riparius*	96 hr	9.2[C] (8.1-11)[A] NOEC: 1.34
DADMAC Ditallow $C_{(16-18)2}$	Snail	*Lymnaea stagnalis*	96 hr	18[C] (15-21)[A] NOEC: 0.32
DADMAC Ditallow $C_{(16-18)2}$	Fish	*Lepomis macrohirus* Bluegill sunfish	96 hr	0.62[C] (0.45-0.85)[A]
DADMAC Ditallow $C_{(16-18)2}$	Fish	*Lasterosteus aculeatus* Stickleback	96 hr	4.5[C] (4.1-4.9)[A] NOEC: 0.58
DADMAC Ditallow $C_{(16-18)2}$	Fish	*Lepomis macrohirus* Bluegill sunfish	96 hr	1.23[C] (0.99-1.54)[A]
DADMAC Dioctadecyl $C_{(18)2}$	Fish	*Lepomis macrohirus* Bluegill sunfish	96 hr	1.04[C] (0.74-1.45)[A]

[A]95% confidence limits

[B]Algaestic concentration, the concentration that inhibits growth, but logarithmic growth will resume, when the algae are resuspended in fresh medium without test substance.

[C]Effect concentration based on measured concentrations.

Table 11: Acute Aquatic Toxicity of Dioctyl Dimethyl Ammonium Chloride (DODAC) and Didecyl Dimethyl Ammonium Chloride (DDAC)

Chemical	Organism	Species	Duration	Endpoint
DODAC	Aves	Bobwhite quail	8 days	LC_{50} 2625 ppm
DODAC	Aves	Mallard duck	14 days	LD_{50} 240 mg/kg/body wt
DODAC	Aves	Mallard duck	8 days	LC_{50} 5000 ppm
DODAC	Aves	Mallard duck	14 days	LD_{50} 186 mg/kg/body wt
DODAC	Crustacea	*Daphnia magna*	48 hours	EC_{50} 0.10 ppm, NOEL 0.03
DODAC	Fish	Bluegill sunfish	96 hours	LC_{50} 5.9 ppm
DODAC	Fish	Channel fish	96 hours	LC_{50} 11.2 ppm
DODAC	Fish	Fathead minnow	96 hours	LC_{50} 5.2 ppm
DODAC	Fish	Rainbow trout	96 hours	LC_{50} 0.7 ppm, NOEL 0.12
DDAC	Aves	Bobwhite quail	8 days	LC_{50} 5620 ppm, NOEL 3180
DDAC	Aves	Bobwhite quail	8 days	LC_{50} 5620 ppm, NOEL 1780
DDAC	Aves	Bobwhite quail	14 days	LD_{50} 217 mg/kg/body wt, NOEL 31
DDAC	Aves	Bobwhite quail	14 days	LD_{50} 54.4 mg/kg/body wt, NOEL 39
DDAC	Aves	Mallard duck	8 days	LC_{50} 5620 ppm, NOEL 562
DDAC	Aves	Mallard duck	14 days	LC_{50} 5620 ppm, NOEL 1780
DDAC	Crustacea	Mysid	96 hours	LC_{50} 69 ppb, NOEL 52
DDAC	Crustacea	*Daphnia magna*	48 hours	LC_{50} 94 ppb, NOEL 74
DDAC	Crustacea	*Daphnia magna*	48 hours	EC_{50} 18 ppb, NOEL 5.6
DDAC	Fish	Bluegill sunfish	96 hours	LC_{50} 320 ppb, NOEL 100
DDAC	Fish	Bluegill sunfish	96 hours	LC_{50} 600 ppb
DDAC	Fish	Coho salmon	96 hours	LC_{50} 1000 ppb, NOEL 590
DDAC	Fish	Rainbow trout	96 hours	LC_{50} 2800 ppb, NOEL 1800
DDAC	Fish	Sheepshead minnow	96 hours	LC_{50} 0.96 ppm, NOEL 0.39
DDAC	Mollusca	Eastern oyster	96 hours	EC_{50} 0.094 ppm, NOEL 0.063
DDAC	Mollusca	Eastern oyster	96 hours	EC_{50} 0.11 ppm, NOEL 0.072

*DODAC CAS No. 5538-94-3
**DDAC CAS No. 7173-51-5

VIII. Aggregate Exposures

Section 408 of the Federal Food, Drug, and Cosmetic Act (FFDCA) requires the US EPA to consider available information concerning exposure from a chemical in food and all other, non-occupational avenues, including that from drinking water and residential or other indoor uses. In the case of the AACSs potential exposure from the FDA-approved uses of these compounds dwarfs that from the pesticidal uses. These compounds are of systemic low toxicity. Consequently, the qualitative assessment provided in this document is appropriate.

IX. Cumulative Exposure:

Section 408(B)(2(D)(v) of the FFDCA requires that, when the US EPA makes decision on a tolerance, the Agency will consider "available information" concerning the cumulative effects of a particular compound and "other substances that have a common mechanism of toxicity." As discussed above, AACSs are structurally related to other classes of chemicals,

all of which are of low-toxicity and which resemble natural products. Consequently, the separate or combined risks are expected to be low.

No information is available that indicates that AACSs share a "common mechanism of toxicity" with other classes of chemicals nor has the EPA made a determination that such a relationship exists. Consequently, for the purposes of reassessing the tolerances of AACSs, no assumption of a common mechanism of toxicity with any other group of chemicals should be made. Reconsideration of this aspect of this review should occur if new information on a common mechanism of toxicity with some other class of chemicals becomes available.

X. Recommendations:

The data reviewed and analyzed in this assessment support the following conclusions:

1. AACSs exhibit limited toxicity to mammals and, therefore, the risks associated with their use in pesticides are of minimal concern. [1-5]
2. Exposure to AACSs from their use in pesticides is likely to be several orders of magnitude less than the exposure in cosmetics, cleansers, and other personal care products that are regulated by the Food and Drug Administration and approved for use by the general population.
3. The data reviewed in this assessment cover AACSs listed in Table 2.

Consequently, the STF recommends that the tolerance exemptions of the AACSs be reassessed and the tolerance expressions listed in 40 CFR Parts 180.910, 920, and 930 should be combined and simplified into two tolerance expressions to read as follows:

Proposed New AACS Tolerance Exemption Expressions

(3-Lauramidopropyl) trimethylammonium methyl sulfate

Mono- and di-alkyl (C_8-C_{18}) methylated quaternary ammonium chloride or methyl sulfate salts and their bis(2-hydroxyethyl) and bis(poly(oxyethylene)) analogs, where the alkyl group(s) (C_8-C_{18}) are derived from coconut, cottonseed, soya, tallow, or hogfat fatty acids.

Because of the potential for AACSs to exhibit eye and/or skin irritation, the STF further recommends that AACSs be placed on EPA Inerts List 4B. It should be noted that the corrosivity findings with certain sulfonic acids are likely due to their low pH. The AACSs used in pesticides are in their ionized form at pHs near neutral.

References:

NOTE: Documents not authored by US EPA staff that are not available on the Internet and have not been previously submitted by the Surfactants Task Force are provided as separate volumes accompanying this submission.

1. Madsen T, *et al.*, Environmental and Health Assessment of Substances in Household Detergents and Cosmetic Detergent Products. Environmental Project No. 615 (2001). [URL: http://www.mst.dk/udgiv/Publications/2001/87-7944-596-9/pdf/87-7944-597-7.pdf]

2. Cosmetic Ingredient Review, Final report on the safety assessment of cetrimonium chloride, cetrimonium bromide, and steartrimonium chloride. *International Journal of Toxicology*, 16 (1997) 195-220.

3. Toxicology/Regulatory Services, Inc. Fatty Nitrogen Derived Cationics Category High Production Volume (HPV) Chemicals Challenge, Test Plan. December 13, 2001. [URL:www.epa.gov/chemrtk/fatnitro/c13407tp.pdf]

4. Various alkyl ammonium chloride salts (CAS No. 112-00-5, 112-02-7, 112-03-8, 107-64-2, 5538-94-3, and 7173-51-5) chemical/physical properties. [URL: www.chemicalland21.com]

5. Yam J, *et al.*, Surfactants: A survey of short-term genotoxicity testing. *Fd. Chem. Toxic.*, Vol. 22, No. 9 (1984) 761-769. [MRID 46551424]

6. Lassen et al., Inventory of Biocides used in Denmark. Environmental Project No. 585 (2001). [URL: http://www.mst.dk/udgiv/Publications/2001/87-7944-383-4/html/kap04_eng.htm]

7. CAS No. 5538-94-3 and 7173-51-5 ecotoxicity, [URL: http://old.ipmcenters.org]

ATTACHMENT A

Resource List

Resource List

National Toxicology Program	ntp-server.niehs.nih.gov
Evaluation of Risks to Human Reproduction	cerhr.niehs.nih.gov
TOXNET	www.toxnet.nlm.nih.gov HSDB IRIS CCRIS GENE-TOX TOXLINE DART/ETIC
GATEWAY	gateway.nlm.nih.gov/gw/Cmd MEDLINE OLDMEDLINE MEDLINEplus DIRLINE
Agency for Tox. Substances and Disease	www.atsdr.cdc.gov/toxprofiles
OSHA/NIOSH	www.cdc.gov/niosh/topics/chemical-safety www.cdc.gov/niosh/npg/npg.html www.cdc.gov/niosh/ipcsneng/neng0000.html www.cdc.gov/niosh/81-123.html
NTIS	www.ntis.gov
Federal Government Organizations	www.firstgov.gov/ www.science.gov/
TSCA Section 4	www.epa.gov/opptintr/chemtest/sumindex.htm
International Agency Research on Cancer	www.iarc.fr
OPPT Fact Sheets	www.epa.gov/opptintr/chemfact/
TSCA Submissions	esc.syrres.com/efdb/TSCATS.htm
High Production Volume Challenge	www.epa.gov/chemrtk/viewsrch.htm
Cosmetic Ingredient Review	www.cir-safety.org/staff_files/publist.pdf
EPA drinking water	www.epa.gov/safewater/mcl.html
INCHEM	www.inchem.org
OECD	cs3-hq.oecd.org/scripts/hpv/
BIBRA	www.bibra.co.uk
EPA Environmental Publications	www.epa.gov/ncepihom/
REDs by OPP	www.epa.gov/pesticides/reregistration/status.htm
Google search engine	www.google.com
Yahoo search engine	www.yahoo.com
Florida university library system	http://webluis.fcla.edu/
Georgia university library system	http://gil.valdosta.edu/
Scientific information search engine	http://www.scirus.com/srsapp/
Elsevier electronic journals	http://www.info.sciencedirect.com